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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/771,151	01/26/2001	Danilo D. Lasic	55325-8169.US00	9729

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ALZA Corporation
1900 Charleston Road, P.O. Box 7210
M10-3
Mountain View, CA 94039-7210

EXAMINER

KISHORE, GOLLAMUDI S

ART UNIT	PAPER NUMBER
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1615

DATE MAILED: 11/05/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/771,151

Applicant(s)
Lasic

Examiner
Gollamudi Kishore, Ph.D

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1615



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jul 30, 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 3-9, and 16 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-9, and 16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other: _____

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DETAILED ACTION

1.137 (b) petition and the filing under 1.114 both dated 7-30-03 are acknowledged.

Claims included in the prosecution are 1, 3-9 and 16.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1, 3-9 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants are claiming a specific method of preparation of liposome and therefore, claim 1 should recite the individual steps. Claim 1 (also claim 16) just recites selecting the compound and the liposomal sizes, but does not recite how the supersaturated solution of the compound is entrapped in the liposomes. How can size of the liposomes by itself does not cause the precipitation of the compound and how is the size selected? This rejection is maintained since applicants have not adequately addressed this specific issue.

Applicant's arguments have been fully considered, but are not found to be persuasive. Instant invention is drawn to a method of encapsulating a supersaturated solution of a compound. According to line 8 of claim 1, the size of the liposomes is selected which size is effective to inhibit the precipitation of the compound. For one to determine

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what sizes inhibit the precipitation, one doesn't have to first encapsulate the supersaturated solution itself in different sizes of liposomes? Applicant point out to page 8, lines 2-29 with regard to this issue. At this location, the examiner is unable to find any disclosure as to how or conditions under which the supersaturated solution is encapsulated. With regard to the issue as to how the size of the liposomes would cause or would not cause the precipitation, applicant points out to page 22 lines 7-15; the examiner is unable to find any disclosure as to the relation between the liposome sizes and the precipitation. On page 8, lines 19-29, applicant's statements appear to indicate that the temperature and pH have an effect on the precipitation. It is still the examiner's position that since the claims are drawn to a method of encapsulation, the method steps should be defined in order to distinctly claim the subject matter which applicant regards as the invention.

It is unclear as to what is being conveyed by "removing from the external liposome suspension medium the condition selected to maintain the compound above the room temperature. For example, the parent claim lists 'solvent pH' as one of the conditions; it is unclear as to how the change of pH would change the temperature as recited in claim 9.

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Claim Rejections - 35 USC § 102

- 3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:**

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

- 4. Claims 1, 3-6, 8 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0177 223.**

- 5. EP discloses a method of preparation of liposomes containing a supersaturated solution of a biologically active compound (note the abstract, page 10, lines 4-5, Examples and claims).**

Applicants' arguments have been fully considered, but are not found to be persuasive. Applicants argue that EP relates to a pharmaceutical multi-phase composition for use as a drug delivery system. This argument is not found to be persuasive since as already pointed out, instant 'comprising' does not exclude the solid form present in the EP liposomes. EP does disclose super-saturated solution of the active agent and hence meets the requirements of instant claims. With regard to the limitation of two fold increase in the water solubility, the examiner points out that the solubility of a compound is a function of temperature and instant claim does not recite any temperature. There is nothing in the prior art which shows that a solubility of two fold cannot be achieved at a given temperature. With regard to applicant's arguments that Mezei's liposomes are spherical,

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The examiner points out that instant claims do not recite the requirement that the liposomes should not be spherical.

6. Claims 1, 3-6, 8-9 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0 551 169.

EP discloses a method of preparation of liposomes containing a supersaturated solution of a water soluble drug (note the abstract, Example 3 and claims).

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that nowhere does Yamamoto teaches selection of liposome sizes in order to maintain the compound in the form of a supersaturated solution. This argument is not persuasive since according to the reference, the supersaturated solution is at the room temperature (see abstract) . This implies that the compound is not in a precipitated state and this in turn means that the liposomes in the reference have a selected liposomal sizes. Applicant arguments pertain to the motive behind the prior art process of encapsulating the supersaturated solution and instant motive. These arguments are not found to be persuasive since the process and the product formed are the same irrespective of the motivation of employing liposomes in instant case.

6. Claims 1, 3-9 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/07409.

WO 98 discloses a method of preparation of liposomes containing supersaturated solution of an active compound. The liposomes further contain a hydrophilic polymer

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(PEG) (note the abstract, page 2 line 15 through page 3, line 24, page 6, lines 14-26, page 12, lines 4-21, Example 3 and claims).

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argue that in WO the drug is entrapped in the inner aqueous compartment in a dissolved or precipitated form and in contrast, applicant's invention specifically employs liposomes that 'inhibit the formation of precipitated drug and employing compounds having room temperature water solubility capable of exhibiting at least a two fold increase in response to a condition where the condition may be (I) increasing the solvent temperature -----'. These arguments are not found to be persuasive for the following reasons. First of all, as recognized by applicants themselves, the reference teaches entrapment of the active agent EITHER in the dissolved or precipitated state. That means the reference teaches instant process of a solubilized compound. With regard to the limitation of two fold increase in the water solubility, the examiner points out that the solubility of a compound is a function of temperature and instant claim does not recite any temperature. There is nothing in the prior art which shows that a solubility of two fold cannot be achieved at a given temperature. The examiner directs applicant's attention to page 12, lines 4-21 wherein the reference teaches a solubility of 8.5 mg/ml of cisplatin which is eight fold (line 10); this implies that the solution is in a supersaturated form. The reference meets the requirements of instant claims.

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Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over either of EP 0 177 223 or EP 0 551 169 in combination with Woodle (5,013,556) of record.

What is lacking in either of the EP references is the inclusion of a hydrophilic polymer in the liposome compositions.

Woodle discloses that the inclusion of a hydrophilic polymer enhances the circulation time of the liposomes (note the abstract).

The inclusion of a hydrophilic polymer in the liposomes of EP references would have been obvious to one of ordinary skill in the art because it enhances the circulation time of the liposomes as taught by Woodle.

Applicants' arguments have been fully considered but are not found to be persuasive. Although applicants admit that Woodle teaches the use of hydrophilic polymer, they argue that it does not overcome the deficiencies of the primary documents. Applicant's arguments with regard to the deficiencies EP references have been addressed above.

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9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.

The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, T.K. Page, can be reached on (703)308-2927. The fax phone number for this Group is (703)305-3592.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].

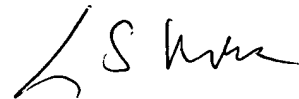
All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-1235.



Gollamudi S. Kishore, Ph. D

Primary Examiner

Group 1600

gsk

November 3, 2003